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CLAIMS

1-37 (Canceled)

38. (Withdrawn) A compound having purity in excess of 98% by HPLC, having the formula:

wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions; and 5 y, and z are each selected from H, a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions and a group that can be attached to a solid support.

39. (Withdrawn) The compound of claim 23, wherein the group that is attachable to a solid support has the formula O-C(=O)-M-C(=O)-NH-Spacer, where M is selected from the group consisting of succinyl, oxalyl, and hydroquinolynyl, and wherein the Spacer is selected from the

40. (Withdrawn) group consisting of a C1-C6 alkyl, ethyloxyglycol, and a combination of alkyl and ethyleneglycoxy.

41. (Withdrawn) A compound having the formula:

wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions; z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and n is 2-20.

42. (Withdrawn) A compound of the formula:

wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions; z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and n is 2-20.

43. (Withdrawn) A compound having a purity in excess of 97% by HPLC, as shown by the formula:

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wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R" are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

44. (Withdrawn) A compound having purity in excess of 97 % by HPLC, and having the formula:

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wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R" are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

45. - 50. (Canceled)

- 51. (Currently Amended) An synthetic oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising at least two CpG moieties and a covalently linked nucleoside antimetabolite covalently linked to the oligonucleotide.
- 52. (Canceled)

- 53. (Currently Amended) An synthetic oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising at least two CpG moieties and a covalently linked nucleoside antimetabolite eovalently linked to the oligonucleotide, wherein, the antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and 2'-deoxy, 2',2'-difluorocytidine.
- 54. (Currently amended) The oligonucleotide of claim 51 or 53, wherein two of said at least two CpG moieties are separated by a number of nucleotides selected from the group of numbers 2, 5, and 9-nucleotides.
- 55. (Previously presented) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 5' to said at least two CpG moieties.
- 56. (Previously presented) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 3' to said at least two CpG moieties.
- 57. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 3' to at least one of said at least two CpG moietyies and 5' to at least a second of said at least two CpG moietyies.
- 58. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-3' linkage.
- 59. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 5'-5' linkage.
- 60. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-5' linkage.

61. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is eovalently linked to the oligonucleotide by a 5'-3' linkage.

62. (Currently amended) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked at a position that is selected from the following positions: 10 nucleotides upstream from one of the said at least two CpG moieties, 9 nucleotides upstream from one of the said at least two CpG moiety moieties, 8 nucleotides upstream from one of the said at least two CpG moiety moieties, 7 nucleotides upstream from one of the said at least two CpG-moiety moieties, 6 nucleotides upstream from one of the said at least two CpG-moiety-moieties, 5 nucleotides upstream from one of the said at least two CpG-moiety-moieties, 4 nucleotides upstream from one of the said at least two CpG-moiety-moieties, 3 nucleotides upstream from one of the said at least two CpG-moiety moieties, 2 nucleotides upstream from one of the said at least two CpG-moiety moieties, 1 nucleotides upstream from one of the said at least two CpG-moiety moieties, 10 nucleotides downstream from ((a)) CpG-moiety moieties, 9 nucleotides downstream from one of the said at least two CpG-moiety moieties, 8 nucleotides downstream from one of the said at least two CpG-moiety_moieties, 7 nucleotides downstream from one of the said at least two CpG-moiety moieties, 6 nucleotides downstream from one of the said at least two CpG-moiety moieties, 5 nucleotides downstream from one of the said at least two CpG-moiety moieties, 4 nucleotides downstream from one of the said at least two CpG-moiety moieties, 3 nucleotides downstream from one of the said at least two CpG moiety moieties, 2 nucleotides downstream from one of the said at least two CpG-moiety moieties, and 1 nucleotides downstream from one of the said at least two CpG-moiety moieties.

63. (Currently amended) The oligonucleotide of claim 51 or 53, wherein the nucleoside antimetabolite is covalently linked to the oligonucleotide by a linker having the formula.

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wherein $\times X$ and Y are independently selected from

and R is selected from the group consisting of H, S, a Ci C₆ C1-C6 alkyl, ((a)) C1-C6 alkoxy, and NH.

- 64. (Previously presented) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.
- 65. (Previously presented) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.
- 66. (Previously presented) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-halogen nucleotide.
- 67. (Currently amended) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide emprises comprising at least one 2'-N-alkyl nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.
- 68. (Currently amended) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises comprising at least one 2'-0-alkyl 2'-O-alkyl nucleotide, one 2'-N-Alkyl 2'-n-alkyl nucleotide, or one 2'-0-halogen nucleotide, wherein the an alkyl has between about 1 and about 6 carbon atoms.
- 69. (Currently amended) The oligonucleotide of claim 68, wherein the each alkyl is methyl.
- 70. (Currently amended) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises comprising a plurality of nucleotides connected by covalent internucleoside internucleotide linkages wherein each of the linkages are selected from the group consisting of

- ((a)) phosphodiester linkage, ((a)) C1-C6 alkoxy phosphotriester linkage, ((a)) phosphorothioate linkage and ((a)) phosphoramidate linkage.
- 71. (Previously presented) A pharmaceutical composition comprising the oligonucleotide of any of claims 51 or 53-70.
- 72. (Previously presented) A pharmaceutical composition of claim 71 further comprising a pharmaceutically acceptable carrier.
- 73. (Previously presented) The oligonucleotide of claim 72 wherein said pharmaceutically acceptable carrier is lipofectin.
- 74. (Currently amended) An <u>synthetic</u> oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein P is a nucleoside antimetabolite and X represents between 0 and 50 nucleotides.
- 75. (Currently amended) An <u>synthetic</u> oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein X represents between 0 and 50 nucleotides and P is a nucleoside antimetabolite selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and 2'-deoxy, 2' -,2' -difluorocytidine.
- 76. (Previously presented) The oligonucleotide of claim of 74 or 75, where X is selected from the group consisting of 2, 5, and 9 nucleotides.

- 77. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple X has at least one nucleotide((s)) and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-3' linkage.
- 78. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple X has at least one nucleotide((s)) and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-5' linkage.
- 79. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple X has at least one nucleotide((s)) and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-5' linkage.
- 80. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 10 multiple nucleotides X has at least one nucleotide((s)) and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-3' linkage.
- 81. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide emprises comprising at least one nucleotide having a ribose sugar moiety.
- 82. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide emprises comprising at least one nucleotide having a 2'-deoxyribose sugar moiety.
- 83. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises comprising at least one 2' 0-alkyl 2'-O-alkyl nucleotide, 2'-N-Alkyl nucleotide, or 2'- 0-halogen 2'-O-halogen nucleotide, wherein the an alkyl has between about 1 and about 6 carbon atoms.
- 84. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide emprises comprising a plurality of nucleotides connected by covalent internucleoside linkages, wherein the linkages are selected from the group consisting of phosphodiester linkage, ((a)) C1-

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C6 alkoxy phosphotriester linkage, ((a)) phosphorothioate linkage and ((a)) phosphoramidate linkage.

85. (Currently amended) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 30 multiple X has at least one nucleotide((s)) and the nucleoside antimetabolite is attached to at least one of the multiple nucleotides by a linker having the formula.

wherein $\times X$ and Y are independently selected from

and R is selected from the group consisting of H, S, a C1-C6 alkyl, a Ci-C₆ a C1-C6 alkoxy, and NH.

- 86. (Previously presented) A pharmaceutical composition comprising the oligonucleotide of any of claims 74-85.
- 87. (Previously presented) A pharmaceutical composition of claim 86 further comprising a pharmaceutically acceptable carrier.
- 88. (Previously presented) The oligonucleotide of claim 87 wherein said pharmaceutically acceptable carrier is lipofectin.
- 89. (Currently Amended) <u>A</u> The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:
 - (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
 - (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties.

90. (Canceled)

- 91. (Currently Amended) <u>A</u> The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:
 - (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
 - (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties,

wherein, said antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and 2'-deoxy, 2',2'-difluorocytidine.

92. (Previously presented) The method of claim 89 or 91, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.